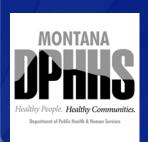
Measles — A Forgotten Disease is Back!

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Sources

The majority of the slides in this presentation are adapted from The Pink Book: Course Textbook — 12th Edition Second Printing http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/12-Meas.pdf

 Other slides were created from VPD Surveillance Manual, 6th Edition, 2013. Measles: Chapter 7-1.

CLINICAL BACKGROUND

Measles

- Highly contagious viral illness
- First described in 7th century
- Near universal infection in childhood in prevaccination era
- Common and often fatal in developing areas



Measles Virus

- Paramyxovirus (RNA)
- Hemagglutinin important surface antigen
- One antigenic type
- Rapidly inactivated by heat and light

Measles Pathogenesis

- Respiratory transmission of virus
- Replication in nasopharynx and regional lymph nodes
- □ Primary viremia 2–3 days after exposure
- Secondary viremia 5–7 days after exposure with spread to tissues
- Can spread illness 4 days before to 4 days after rash onset (minimal after 2nd day following rash onset)

Measles Clinical Features

Incubation period: exposure to rash onset averages
 14 days (range: 7–21 days)

Prodrome

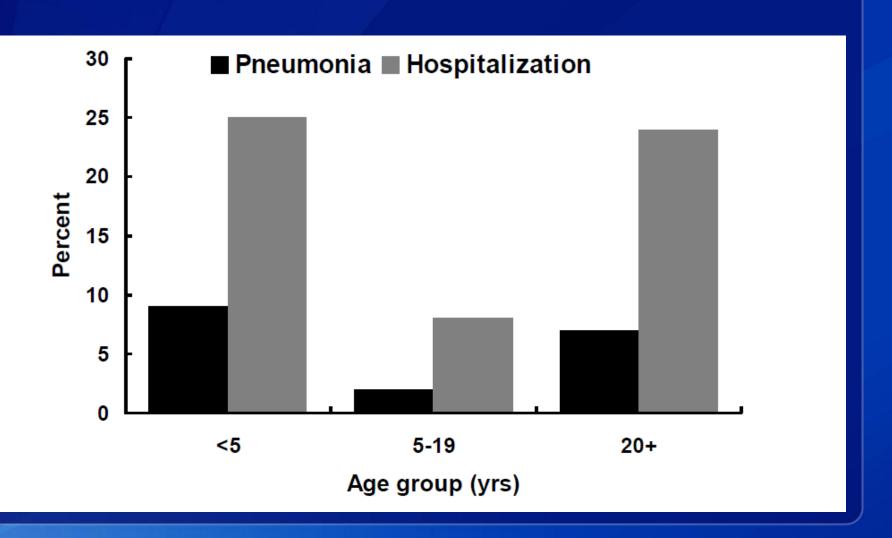
- Stepwise increase in fever to 103°F or higher
- Cough, coryza, conjunctivitis
- Koplik spots (rash on mucous membranes)



Measles Complications

Condition	Percent reported	
Diarrhea	8	
Otitis media	7	
Pneumonia	6	
Encephalitis	0.1	
Hospitalization	18	
Death	0.2	

Measles Complications by Age Group



Measles Laboratory Diagnosis

- □ Detection of RNA by RT-PCR
- Positive serologic test for measles IgM antibody
- Isolation of measles virus from a clinical specimen (e.g., nasopharynx, urine)
- Significant rise in measles IgG by any standard serologic assay (e.g., EIA, HA)
- Genotype testing

Measles Testing

- Laboratory confirmation is essential for all outbreaks and sporadic cases
- Efforts should be made to obtain serum sample, throat swab (or nasopharyngeal swab) +/- urine sample at first contact with suspect measles case
- Measles is rare, so false-positive IgM's are possible must restrict testing to patients most likely to have measles (i.e., meet clinical case definition)

Measles Testing at DPHHS



Montana Public Health Laboratory Guidance on Measles Testina

Specimen Criteria

Collect the following specimens to test for measles infection:

- Respiratory Specimen* (Throat, NP, Nasal Swab)
- Urine
- Serum tests will only be performed for IgG and IgM if the PCR result is not definitive

 If only one specimen is obtained, the respiratory specimen in viral transport media is the most important.

Specimen Collection for PCR Testing:

Collect specimens as soon as possible after appearance of rash, and ideally within 3 days of rash onset. Detection can be possible up to day 7 following onset of rash. Collection of urine increases the likelihood of detecting the virus.

- Respiratory Specimen: Throat, Nasopharyngeal or Nasal Dacron swabs in viral transport media.
 Urine: 10-50 ml of urine collected in a sterile container, processed by centrifuging at 500 x g for
- 15 minutes at 4°C. Resuspend the sediment in 2-3 ml of viral transport medium.

Consult with Public Health authorities regarding PCR testing <u>prior to rash</u> development of individuals who may have had a recent exposure to measles.

Specimen Collection for IgG and IgM Testing:

For IgM testing, specimens must be collected >48 hours post rash onset.

 Serum: 1 – 2 ml of serum. Can be sent in a spun serum separator tube, or can be poured off into a transport tube.

Transport Conditions:

- Keep PCR specimens cold, and transport with cold packs as soon as possible following specimen
 collection. Avoid repeat freeze-thaw cycles or freezing at -20°C. If specimen transport is going
 to be delayed, freeze the sample at -70°C and ship on dry ice. If -70°C is not available, it is better
 to maintain the specimen at 4°C.
- . Serum specimens can be shipped cold (preferable) or at room temperature.

Submission Reminders

Complete a blue MTPHL laboratory requisition, and be sure to include the date of rash onset, along with the collection date and two patient identifiers (Name and DOB or medical record#)

Specimens can be transported by courier (if available), UPS, or FedEx to:

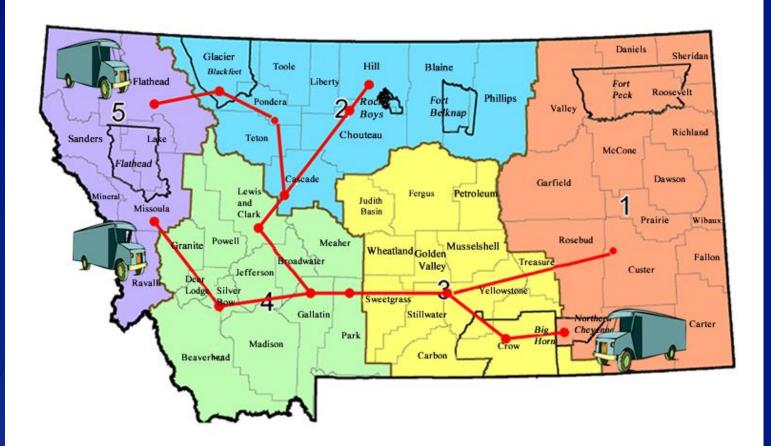
Montana Public Health Laboratory Montana Public Health Laboratory
1400 Broadway or PO Box 4369

1400 Broadway or PO Box 4369
Helena, MT 59601 Helena, MT 59601

Please contact the Montana Public Health Laboratory at 1-800-821-7284 for more information and remember to report any suspect measles to your local health department.

Montana Public Health Laboratory Guidance for Measles Testing, Revised 02/2015

Courier Routes



Call Montana Laboratory Services Bureau at (800) 821-7284 for any problems with Courier or to arrange for Speciman Pickup

EPIDEMIOLOGY

Measles Epidemiology

Reservoir Human

Transmission Respiratory

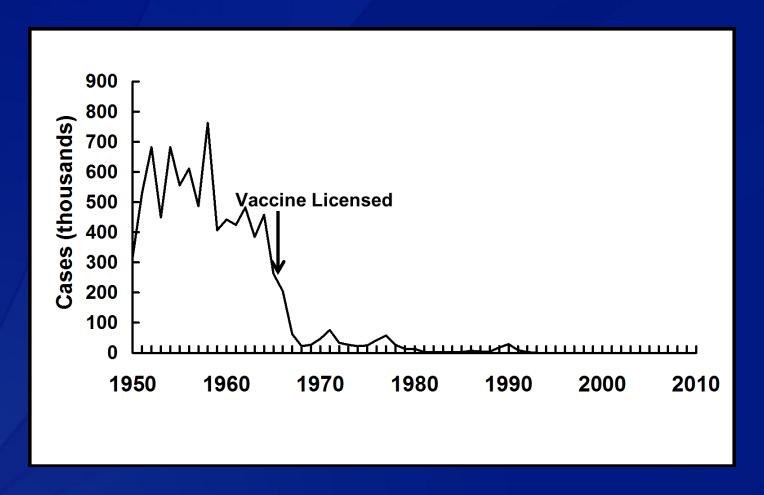
Airborne

Temporal pattern Peaks in late Winter-Spring

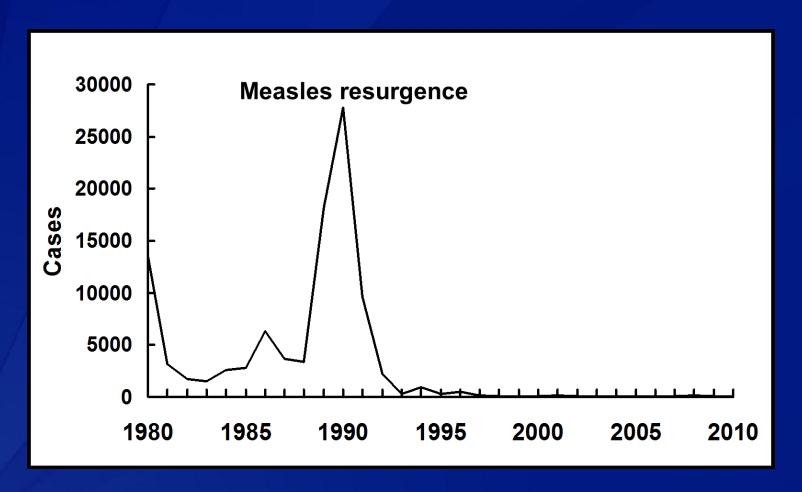
Communicability 4 days before to 4 days

after rash onset

Measles — United States, 1950-2010



Measles — United States, 1980–2010



Measles Resurgence — United States, 1989-1991

□ Cases 55,622

Age group affected Children aged <5 yrs</p>

■ Hospitalizations >11,000

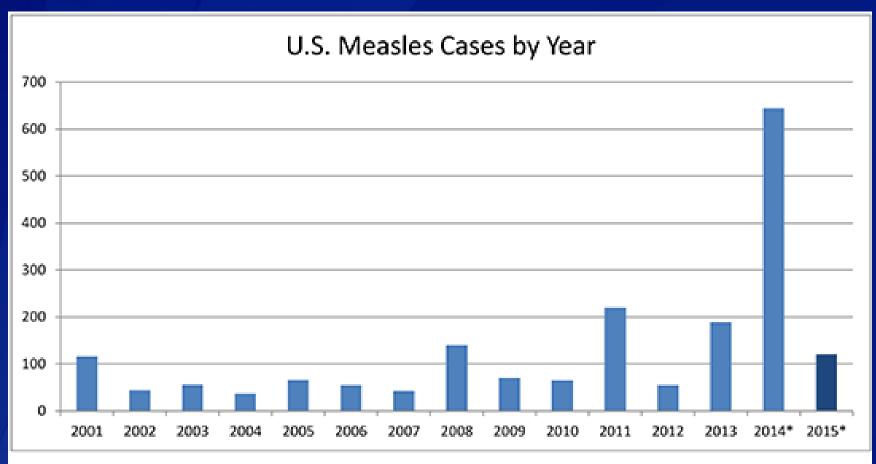
Deaths123

Direct medical costs >\$150 million

Measles 1993-2009

- Endemic transmission interrupted
- Record low annual total in 2004 (37 total cases)
- Many cases among adults
- Most cases imported or linked to importation
- Most persons with measles were unvaccinated or unknown vaccination status

Measles Cases — United States, 2001–2015

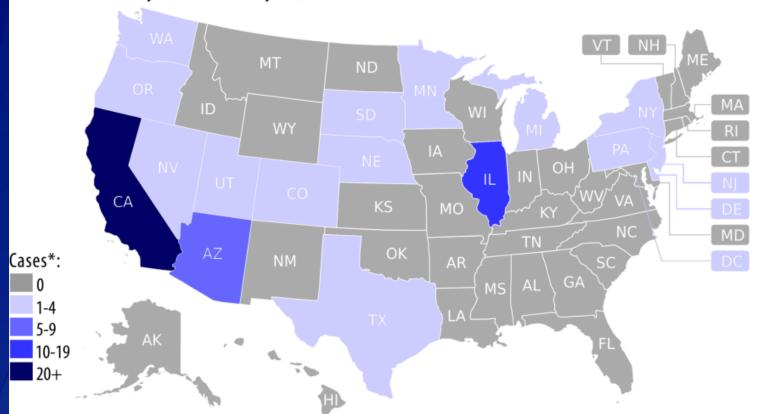


*Provisional data reported to CDC's National Center for Immunization and Respiratory Diseases

http://www.cdc.gov/measles/cases-outbreaks.html

2015 Measles Cases in the U.S.

January 1 to February 13, 2015



From January 1 to February 13, 2015, 141 people from 17 states and Washington DC [AZ (7), CA (98), CO (1), DC (1), DE (1), IL (11), MI (1), MN (1), NE (2), NJ (1), NY (2), NV (4), OR (1), PA (1), SD (2) TX (1), UT (2), WA (4)] were reported to have measles*. Most of these cases are part of a large, ongoing, multi-state outbreak linked to an amusement park in California.

*Provisional data reported to CDC's National Center for Immunization and Respiratory Diseases



Measles Case Definition (2013)

Clinical Description

- Acute illness characterized by:
 - Generalized maculopapular rash lasting ≥3 days; and
 - Temperature ≥101°F or 38.3°C; and
 - Cough, coryza, or conjunctivitis

Measles Case Definition (2013) — Case Classification

Probable

- In the absence of a more likely diagnosis, an illness that meets the clinical description with:
 - No epidemiologic linkage to a laboratory-confirmed measles case; and
 - Noncontributory or no measles laboratory testing.

Measles Case Definition (2013) — Case Classification

Confirmed

- An acute febrile rash illness with:
 - Isolation of measles virus from a clinical specimen; or
 - Detection of measles-virus specific nucleic acid from a clinical specimen using PCR; or
 - IgG seroconversion or a significant rise in measles IgG using any evaluated and validated method; or
 - A positive serologic test for measles IgM; or
 - Direct epidemiologic linkage to a case confirmed by one of the methods above.

Note: temperature does not need to reach $\geq 101^{\circ}F/38.3^{\circ}C$ and rash does not need to last for ≥ 3 days.

Epidemiologic Classification of U.S. Cases

1. Import-linked case

Any case in a chain of transmission epidemiologically linked to an internationally imported case

2. Imported-virus case

A case for which an epidemiologic link to an internationally imported case was not identified, but for which viral genetic evidence indicates an imported measles genotype, i.e., a genotype that is not occurring within the United States in a pattern indicative of endemic transmission.

Epidemiologic Classification of U.S. Cases

3. Endemic case

A case for which epidemiological or virological evidence indicates an endemic chain of transmission. Endemic transmission is defined as a chain of measles virus transmission that is continuous for ≥12 months within the United States.

4. Unknown source case

A case for which an epidemiological or virological link to importation or to endemic transmission within the U.S. cannot be established after a thorough investigation. These cases must be carefully assessed epidemiologically to assure that they do not represent a sustained U.S.-acquired chain of transmission or an endemic chain of transmission within the U.S

http://wwwn.cdc.gov/NNDSS/script/casedef.aspx?CondYrID=908&DatePub=2013-01-01

VACCINES

Measles Vaccines

1963	Live attenuated and killed vaccines	
1965	Live further attenuated vaccine	
1967	Killed vaccine withdrawn	
1968	Live further attenuated vaccine (Edmonton-Enders strain)	
1971	Licensure of combined measles-mumps- rubella vaccine	
1989	Two dose schedule	
2005	Licensure of MMRV	

Measles Vaccine

Composition Live virus

Efficacy 95% (range, 90%-98%)

Duration of Immunity Lifelong

Schedule2 doses

- Should be administered with mumps and rubella as MMR or with mumps, rubella and varicella as MMRV
- Single antigen vaccines are not available in U.S.

MMRV (ProQuad)

- Combination measles, mumps, rubella and varicella vaccine
- Approved for children aged 12 months-12 years (up to age 13 years)
- Titer of varicella vaccine virus in MMRV is more than
 7-times higher than standard varicella vaccine

MMR Vaccine Failure

- Measles, mumps, or rubella disease (or lack of immunity) in a previously vaccinated person
- 2%-5% of recipients do not respond to the first dose
- Caused by antibody, damaged vaccine, record errors
- Most persons with vaccine failure will respond to second dose

Measles (MMR) Vaccine Indications

- All children aged 12 months and older
- Susceptible adolescents and adults without documented evidence of immunity

Measles Mumps Rubella (MMR) Vaccine

- Minimum age: 12 months
- MMR given before age 12 months should not be counted as a valid dose
- Revaccinate at age ≥12 months

Second Dose of Measles Vaccine

- Intended to produce immunity in persons who failed to respond to the first dose (primary vaccine failure)
- May boost antibody titers in some persons
- First dose of MMR at 12–15 months
- Second dose of MMR at 4–6 years
- Second dose may be given any time at least 4 weeks after the first dose

Adults at Increased Risk of Measles

- College students
- International travelers
- Healthcare personnel

Acceptable Evidence of Immunity to Measles

Routine	Students at post- high school educational institutions	Healthcare Personnel	International Travelers
Documentation of receiving live measles vaccine (1) Preschool (1 dose) (2) K-12 (2 doses) (3) Adults not at highrisk (1 dose)	Documentation of receiving 2 doses of live measles vaccine	Documentation of receiving 2 doses of live measles vaccine	Documentation of receiving live measles vaccine (1) Infants aged 6–11 months (1 dose) (2) Persons aged ≥12 months (2 doses)
Laboratory evidence of immunity	Laboratory evidence of immunity	Laboratory evidence of immunity	Laboratory evidence of immunity
Laboratory confirmation of disease	Laboratory confirmation of disease	Laboratory confirmation of disease	Laboratory confirmation of disease
Born before 1957	Born before 1957	Born before 1957 (healthcare institutions should consider vaccinating those with 2 doses of MMR if no evidence of immunity)	Born before 1957

Measles Vaccine Indications for Revaccination

- Vaccinated before the first birthday
 (e.g., vaccinated in error, before international travel)
- Vaccinated with killed measles vaccine
- Vaccinated prior to 1968 with an unknown type of vaccine
- Vaccinated with IG in addition to a further attenuated strain or vaccine of unknown type

MMR Vaccine Contraindications and Precautions

- Severe allergic reaction to vaccine component or following prior dose
- Pregnancy
- Immunosuppression
- Moderate or severe acute illness
- Recent blood product
- Personal or family (i.e., sibling or parent) history of seizures of any etiology (MMRV only)

MMR Adverse Reactions

□ Fever* 5%-15%

□ Rash* 5%

Joint symptoms25%

□ Thrombocytopenia* <1/30,000 doses

Parotitis rare

Deafness rare

Encephalopathy* <1/1,000,000 doses</p>

^{*}Reactions usually attributed to the measles component

MMRV Adverse Reactions

MMRV has higher risk for fever and febrile seizures
 5-12 days after the first dose among children
 aged 12-23 months

One additional febrile seizure for every 2,300–2,600
 MMRV vaccine doses administered

MMR Vaccine and Autism

 There is no scientific evidence that the risk of autism is higher among children who receive measles or MMR vaccine than among unvaccinated children

"The evidence favors a rejection of a causal relationship at the population level between MMR vaccine and autism spectrum disorders (ASD)."

-Institute of Medicine, April 2001

MMR Vaccination Coverage National Immunization Survey, U.S., 1995-2013

■ MMR 1+ (19-35 mo) ■ MMR 2+ (13-17 yr)



NIS data available at http://www.cdc.gov/vaccines/imz-managers/coverage/imz-coverage.html

Clusters of Unvaccinated Persons

 http://www.theguardian.com/society/nginteractive/2015/feb/05/-sp-watch-how-measlesoutbreak-spreads-when-kids-get-vaccinated

Post-exposure Prophylaxis

- Intramuscular immune globulin (IGIM)
- Intravenous IG (IGIV)
- Subcutanous IG (IGSC)
- MMR vaccine
- Recipients should be monitored for signs of measles for 21 days

Intramuscular Immune Globulin (IGIM)

- Give as early as possible after exposure can modify disease course if given within 6 days
 - 0.5 ml/kg
 - Maximum volume = 15 ml
 - Persons >30 kg will receive less than recommended dose
- All infants aged <12 months</p>
- Not for use in controlling outbreaks

Intravenous Immune globulin (IGIV)

- Larger dose can be used compared with IGIM (400 mg/kg)
- Pregnant women without evidence of immunity because at higher risk for severe measles and complications
- All persons with severely compromised immune systems who are exposed to measles regardless of immunologic or vaccination status because they might not be protected
- High-cost
- Extended observation in specialized settings by skilled professionals required

Subcutanous IG (IGSC)

- Available since 2006
- Same major indication as IVIG
- Administration requires pump and advanced training
- Multiple consecutive weekly doses needed to establish steady-state levels

MMR

- Must be given within 72 hours for post-exposure prophylaxis
- Recommended for persons aged ≥6 months
- Except in healthcare settings, persons receiving their first dose of MMR vaccine within 72 hours after exposure may return to school, childcare, or work

OUTBREAK RESPONSE

Case and Contact Investigation

- A single case of measles is a public health priority
- Healthcare providers should report suspect cases of measles IMMEDIATELY to the local health department (ARM 37.114.101)
- Local health departments should report suspected cases of measles to DPHHS within 24 hours (ARM 37.114.101) Call 24/7 at 406-444-0273
- Prompt recognition, reporting, and investigation of measles cases can limit spread of Measles virus

Case and Contact Investigation

- Identify cases and establish diagnosis
- Obtain accurate and complete immunization histories
- Identify source of infection (e.g., travel history, contacts, genotyping)
- Assess potential for transmission and identify contacts without presumptive evidence of immunity
 - Health alerts
 - Active surveillance

Measles Exposure

- Sharing same airspace with person infectious with measles (4 days before to 4 days after rash onset)
- Same classroom, home, clinic, waiting room, airplane, etc. when infectious person was present or 2 hours after person was present*
- No minimum exposure time established (increased exposure time likely increases rate of transmission)

*Only 1 documented case of measles transmission >60 minutes

Measles Surveillance Worksheet

1	Measles Su	ırveilland	e Worksheet		APPENDIX 7
NAME (Last, First)				Hospital Reco	ord No.
Address (Street and No.)	City	С	ounty 2	ZIp	Phone
Reporting Physician/Nurse/Hospital/Clinic/Lab Address					Phone
PETAG	and anti-time				
DETACH HERE and transmit only lower portion if sent to CDC					
County	State			ZIp	
Age Type Age	t months Ethni	I = Hispanic I = Not Hispanic I = Unknown	Race N = Native Amer/Alaskar A = Asian/Pacific Islande B = African American	n Native W = White or O = Other U = Unknown	Sex M = Male F = Female U = Unknown
1 = Onset Date 5 = Re 2 = Diagnosis Date M9 3 = Lab Yest Done 9 = Un	eported to County ported to State or #WR Report Date known	Outbreak Associated Unk = 999	Reported Month Day Year	Imported 1 = Indigenou 2 = Internatio 3 = Out of Stat 9 = Unknown	asi 2 = Probable 3 = Suspect 9 = Unknown
V = Yes N = No N	0 - 30 Days 99 = Unknown ded, Highest ured Temp.	Otitis?	N = No	Pneumonia Y = Yes N = No U = Unio	Y=Yes N=No
Rash Generalized? Fever?	ded, Highest ured Temp.	Thrombo		n? Oth	er Complications? Y = Yes N = No U = Unknown
Y-Yes Y-Yes N-No	unctivitis? (= Yes 4 = No J = Unknown	Y-Y-N	0 - 99 sknown	8 Unknown	es, Please Specify:
Was Laboratory Testing For Measies Done? V = Yes N = No U = Unknown			17 (Received measures accoine?) Y = Yes No U = Unknow	The Reason	cinated, What Was in? (See Reason Codes Below) spe and Manut Codes Below)
Date igM Result Specimen Taken N = Positive N = Regultve I = Incident mission	200	Month E	Type I	Manuf [Lot Number
Date IgG Acute Date IgG Convo Specimen Taken Specimen To	alescent aken				
Mouth Day Year Mouth Day Year Other Lab Result P = Poutitive P = Poutitive N = No Significant Rise in IgG = In-distinguized U = Unidopeen = In-distinguized U = Unidopeen		Number of Soder Federate Number of Soder Federate Pending Pending Hat Done If Yeaconsted BEFORE 1st birthday, If Yeaconsted BEFORE 1st birthday, If Undocome but no doses given ON or AFTER 1st 6 - Under Age For Vaccination			
E = Pending x = Net Done U = Unknown		If received o	at was the reason? ne dose after 1st birthday, selved 2nd dose after 1st at was the reason?	Vaccine Type C A = MMR B = Measles O = Other U = Unknown	odes Vaccine Manuf. Codes M = Merck O = Other U = Unknown
Date First Reported to a Health Depart			Month	Day Year	
Transmission Setting (Where old this case acquire measlers) 1 - to the set of the set o			Outbreak Related? Y = Yes N = No U = Unknown Source of Exposure Fo	If Yes, Outbreak	Enter State ID if source was an
		nong Those The	in-state case; enter Country 8 state) Epi-Linked to Another Confirmed or Probable	Is Case Trac	ter State if source was out-of-
Y = Yes N = No. N = No.			C386? Y - Yes N = No U = Unknown	Generations Import?	to an International Y = Yes N = No U = Unknown

Mother's Name	Father's Name			
Phone				
DETACE	H HERE			
The information below is epidemiologically important, but not included on NETSS screens				
Activity History For 18 Days Before Rash Onset and 7 Days A	Ifter Rash Onset			
Day -18				
Day -17				
Day -16				
Day -15				
Day -14				
Day -13				
Day -12				
Day -11				
Day -10				
Day -9				
Day -8				
Day -7				
Day -6				
Day -5				
Day -4				
Day -3				
Day -2				
Day -1				
Day 0 (Rash Onset)				
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
Day 6				
Day 7				
Clinical Case Definition*: A generalized rash lasting ≥ 3 days, a temperature ≥ 101.0° F	(≥38.3° C), and cough, coryza, or conjunctivitis.			
epidemiologically linked to a confirmed case.	noncontributory or no serologic or virologic testing, and is no			
Confirmed: A case that is laboratory confirmed or that meets a confirmed case. A laboratory-confirmed case does not nee	the clinical case definition and is epidemiologically-linked to d to meet the clinical case definition.			

Control Measures

- Effective control measures rely upon epidemiologic data rather than targeting entire community
- Epidemiologic investigation
- Investigation resources
 - Local and tribal health departments
 - Montana DPHHS
 - Centers for Disease Control and Prevention

Measles in Schools, Colleges, and Other Institutions

- Close contact increases risk for spread
- Control measures very important
 - Exclusion and isolation of cases (can return 5th day after rash onset if not immunocompromised)
 - Offering MMR to those not up-to-date
 - Immunoglobulin if immunocompromised
 - Persons exempted or refusing vaccination should be excluded for 21 days after rash onset in last case of measles

Exclusion From Schools

MCA 20-5-405

(3) Whenever there is good cause to believe that a person for whom an exemption has been filed under this section has a disease or has been exposed to a disease listed in 20-5-403 or will as the result of school attendance be exposed to the disease, the person may be excluded from the school by the local health officer or the department until the excluding authority is satisfied that the person no longer risks contracting or transmitting that disease

Prevention of Measles Spread in Healthcare Settings When a Measles Case Occurs

- Immediate review of evidence of measles immunity for all staff and volunteers
- Exclusion of all healthcare workers (HCW) with active measles cases
- HCWs without presumptive evidence of immunity should be offered the first dose of MMR vaccine and excluded from work day 5 to 21 following exposure
- Isolation of patient in whom measles is suspected in negative air pressure isolation room
- Implementation of airborne precautions

Keys to Measles Control

- Ensuring susceptible persons are vaccinated per ACIP recommendations → vaccination is the key to eliminating measles transmission!!!!!!
- Considering the diagnosis of measles in clinically compatible cases
- □ Reporting suspected measles cases in timely fashion
- Investigating each case of measles thoroughly and promptly

QUESTIONS?

MMR and MMRV Vaccine

- For the 1st dose of measles, mumps, rubella, and varicella vaccines either MMR and varicella vaccines or MMRV vaccine can be used
- Providers should discuss the benefits and risks of both vaccination options with the parents or caregivers
- Unless the parent or caregiver expresses preference for MMRV, CDC recommends using MMR and varicella vaccines for the first dose.
- Providers facing barriers to communicating benefits and risks for any reason, such as language barriers, should administer MMR and varicella vaccines separately

MMR and MMRV Vaccine

- Providers facing barriers to communicating benefits and risks for any reason, such as language barriers, should administer MMR and varicella vaccines separately
- □ For the first dose of measles, mumps, rubella, and varicella vaccines administered at age ≥48 months, and for second dose at any age, use of MMRV vaccine generally is preferred over separate injections of MMR and varicella vaccines

Measles and Mumps Vaccines and Egg Allergy

 Measles and mumps viruses grown in chick embryo fibroblast culture

 Studies have demonstrated safety of MMR in egg allergic children

Vaccinate without testing

Vaccine Storage and Handling MMR Vaccine

- □ Store between 35–46°F (2–8°C) (may be stored in the freezer)
- Store diluent at room temperature or refrigerate
- Protect vaccine from light
- Discard if not used within 8 hours reconstitution

Vaccine Storage and Handling MMRV Vaccine

- Must be stored at an average temperature of 5°F (15°C) or colder at all times
- May be stored at refrigerator temperature for up to 72 hours but must then be discarded if not used (do not refreeze)
- Must be administered within 30 minutes of reconstitution or must be discarded

Measles Vaccine and HIV Infection

- MMR recommended for persons with asymptomatic and mildly symptomatic HIV infection
- NOT recommended for those with evidence of severe immunosuppression
- HIV testing before vaccination is not recommended
- MMRV not approved for use in persons with HIV infection

Tuberculin Skin Testing (TST) and Measles Vaccine

- Apply TST at same visit as MMR
- Delay TST at least 4 weeks if MMR given first
- Apply TST first and administer MMR when skin test read (least favored option because receipt of MMR is delayed)